LBR gene

lamin B receptor

Normal Function

The *LBR* gene provides instructions for making a protein called the lamin B receptor. Different regions (domains) of this protein give it two distinct functions.

One region of the protein, called the sterol reductase domain, gives the protein sterol reductase function (specifically Δ14-sterol reductase function). This function of the lamin B receptor plays an important role in the production (synthesis) of cholesterol. Cholesterol is a lipid (fat) that is obtained from foods that come from animals: eggs, meat, fish, and dairy products. The body also makes (synthesizes) its own cholesterol. During cholesterol synthesis, the sterol reductase function of the lamin B receptor allows the protein to perform one of several chemical reactions that convert a molecule called lanosterol to cholesterol.

The body needs cholesterol to develop and function normally. Before birth, cholesterol interacts with signaling proteins that control early development of the brain, limbs, genitals, and other structures. It is also an important component of cell membranes and myelin, the fatty covering that insulates nerve cells. Additionally, cholesterol is used to make certain hormones and is important for the production of acids used in digestion (bile acids).

Another region of the lamin B receptor, called the DNA-binding domain, attaches (binds) to chromatin, the complex of DNA and proteins that packages DNA into chromosomes. The lamin B receptor can be found in the membrane that surrounds the nucleus (the nuclear envelope). The protein's interaction with chromatin attaches it to the nuclear envelope and helps maintain the chromatin's structure. Proper interaction of chromatin with the nuclear envelope may play a role in several important cellular functions such as making new copies of DNA (replication), controlling the activity of genes, and regulating programmed cell death (apoptosis). The DNA-binding domain of the protein also plays a role in the formation of the nucleus within cells.

Health Conditions Related to Genetic Changes

Greenberg dysplasia

Several mutations in the *LBR* gene have been found to cause Greenberg dysplasia. This severe condition is characterized by abnormal bone formation and is fatal before birth. Research suggests that this condition is caused by the loss of the sterol reductase function of the lamin B receptor. Some *LBR* gene mutations that cause

Greenberg dysplasia change single protein building blocks (amino acids) in the sterol reductase domain of the lamin B receptor, which leads to the loss of sterol reductase activity. Other mutations lead to an abnormally short protein that is likely nonfunctional.

Loss of the sterol reductase function of the lamin B receptor disrupts the normal synthesis of cholesterol within cells. Absence of this function may also allow potentially toxic byproducts of cholesterol synthesis to build up in the body's tissues. Researchers suspect that low cholesterol levels or an accumulation of other substances disrupts the growth and development of many parts of the body. It is not known, however, how a disturbance of cholesterol synthesis leads to the specific features of Greenberg dysplasia.

other disorders

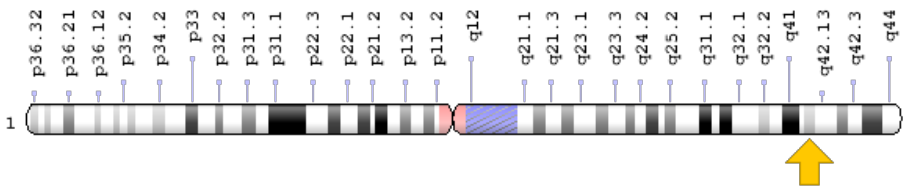
Mutations in the *LBR* gene can also cause Pelger-Huët anomaly, a condition that affects the shape of the nucleus and the structure of chromatin in certain cells but causes no outward signs or symptoms. The nuclei of blood cells called granulocytes normally have multiple segments (or lobes). In contrast, the nuclei of granulocytes in people with Pelger-Huët anomaly have fewer segments than normal (they are hypolobulated). In addition, the chromatin in affected cells appears coarser than usual when viewed under a microscope.

Mutations that cause Pelger-Huët anomaly usually lead to an abnormally short lamin B receptor and reduce the amount of functional protein. It is thought that impairment of the receptor's DNA-binding domain leads to this condition.

Chromosomal Location

Cytogenetic Location: 1q42.12, which is the long (q) arm of chromosome 1 at position 42.12

Molecular Location: base pairs 225,401,502 to 225,428,855 on chromosome 1 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- DHCR14B
- integral nuclear envelope inner membrane protein
- lamin-B receptor
- LBR_HUMAN
- LMN2R
- PHA
- TDRD18

Additional Information & Resources

Educational Resources

- Madame Curie Bioscience Database (2000): Dynamic Connections of Nuclear Envelope Proteins to Chromatin and the Nuclear Matrix
  https://www.ncbi.nlm.nih.gov/books/NBK6125/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28LBR%5BTIAB%5D%29+OR+%28lamin+B+receptor%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- LAMIN B RECEPTOR
  http://omim.org/entry/600024
- PELGER-HUET ANOMALY
  http://omim.org/entry/169400

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_LBR.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=LBR%5Bgene%5D
- HGNC Gene Family: Tudor domain containing
  http://www.genenames.org/cgi-bin/genefamilies/set/780

- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=6518
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/3930
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  http://www.uniprot.org/uniprot/Q14739

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